A31

ASSOCIATIONS BETWEEN BODY MASS INDEX, BODY COMPOSITION, FAT DISTRIBUTION AND KNEE SYMPTOMS SEVERITY IN AFRICAN-AMERICAN AND CAUCASIAN WOMEN

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Aim: We have previously shown that body mass index (BMI) and measures of body composition and fat distribution are associated with radiographic knee OA, but whether these measures are associated with knee symptoms severity is unknown. The purpose of this analysis is to explore the associations between BMI, measures of body composition (fat mass, lean mass, and bone mass), and measures of fat distribution (waist-to-hip ratio and waist circumference) and knee symptoms severity, and to determine whether these relationships are modified by ethnicity.
Methods: Data were from a subset of women (n = 756, 27.5% African-American) aged 45 and older enrolled in the Johnston County Osteoarthritis Project who had available knee radiographs, full body dual-energy x-ray absorptiometry (DEXA) scans, and information on knee symptoms (pain, aching, or stiffness on most days in at least one knee). Six separate proportional odds models were used to examine associations between knee symptoms severity (none, mild, moderate, or severe) and BMI, body composition, and fat distribution variables, modeled in quartiles with adjusted odds ratios and 95% confidence intervals [aOR (95% CI)] calculated comparing the fourth to first quartiles. All models were adjusted for age, ethnicity, prior joint injury, type of DEXA scanner, and Kellgren-Lawrence radiographic grade. Interactions between exposure variables and ethnicity (African-American/Caucasian) were assessed.
Results: Mean (SD) age was 64.6 years (9.3) and BMI 30.2 (6.3). Of the 356 (47.1%) individuals who reported knee symptoms, 37.9%, 40.7%, and 21.3% reported mild, moderate, or severe symptoms, respectively. Adjusted models showed that BMI [aOR=2.41 (1.58, 3.69)], fat mass [aOR=2.11 (1.38, 3.21)], and waist circumference [aOR=1.79 (1.18, 2.70)] were associated with greater cumulative odds of having more severe knee symptoms. Lean mass [aOR=1.36 (0.85, 2.19)], bone mass [aOR=1.17 (0.70, 1.95)], and waist-to-hip ratio [aOR=1.14 (0.75, 1.74)] were not strongly associated with more severe symptoms. No significant interactions were found between BMI, body composition, or fat distribution measures and ethnicity.
Conclusions: In contrast to the associations with radiographic knee OA, increased lean mass and bone mass tend not to be associated with more severe knee symptoms. However, increased BMI, fat mass, and waist circumference are associated with more severe knee symptoms, independently of radiographic severity, in both African-American and Caucasian women. This suggests that the adiposity component of body composition may be more relevant to knee symptoms severity than either lean or bone components, and that interventions targeting adiposity should be emphasized to reduce the burden of knee symptoms in women.

A32

INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN-3: RELATION TO IGF LEVELS AND NUCLEAR LOCALIZATION DURING HUMAN OSTEOARTHRITIS

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Background: Several studies have shown an increase in Insulin-like growth factor (IGF) binding protein 3 (IGFBP-3) in intact osteoarthritic (OA) cartilages and/or cultured OA chondrocytes. IGFBP-3 is a pleitropic protein that can act by modulating IGF signaling via the IGF-I receptor or via IGF independent routes, and its mechanism of action in articular cartilage is unknown.
Goals: (1) To evaluate the relationship between IGFBP-3 and IGF-I levels in extracts of human cartilage derived from donors with different degrees of OA, and (2) to determine the localization of IGFBP-3 in normal and OA cartilage.
Methods: Human cartilage was dissected from femoral heads derived from arthroplasty for OA; severely fibrillated tissues were pooled together, as were mildy-fibrillated and intact areas. All samples (n=17) were evaluated for OA stage by the histological criteria of Mankin. Cartilage extracts were prepared from fresh cartilage samples by stirring in buffers containing 8 M urea, and the extracts depleted of proteoglycans by DEAE chromatography. Total IGF-I was evaluated by ELISA after removal of binding proteins by acid-ethanol extraction, and IGFBP-3 was also evaluated by ELISA (DSLabs). Western Ligand Blots used ^{125}I-IGF-II as the probe. Immunohistochemistry was performed on paraffin embedded sections using polyclonal anti-IGFBP-3 (Upstate).
Results: Normal to mildy degenerated cartilage (scores 0-3) had a mean 2.9 $\pm$ 1.7 ng IGF-I/mg protein (n=6) and OA cartilage (scores $>$ 3) had a mean 3.4 $\pm$ 1.7 (n=11). The correlation of IGF-I to OA group was not statistically significant. IGFBP-3 was measured in the same samples and the molar ratios of IGF-I to IGFBP-3 were calculated. Most of the samples (n=10) had ratios $>$1, indicating an excess of the IGF-I ligand. Two way ANOVA indicated that there were no significant effects between the IGF-I to IGFBP-3 molar ratio and OA group. Western ligand blots of chondrocyte lysates from 2 of the samples showed a stronger signal for IGFBP-3 than the corresponding extracts from intact cartilage (same protein loads). Immunohistochemistry showed a strong intracellular IGFBP-3 signal for a set of 3 samples with mild (score=1), intermediate (score=6) and severe OA (score=10). High resolution imaging indicated that most of the signal was in the cell nucleus, although a web-like cytoplasmic pattern was also noted. The radial zone of normal cartilage was negative, while all zones in OA cartilage were positive. Controls prepared without primary antibody or epitope blocked antibody were all negative.
Conclusions: The excess of IGF-I over IGFBP-3 in OA cartilage and the predominantly nuclear localization of IGFBP-3 strongly suggest that the action of IGFBP-3 is independent of IGF-I receptor signaling. This suggests the hypothesis that IGFBP-3 acts directly through gene regulation of chondrocytes.
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